

Application No. 09/678,202

Amendment dated November 24, 2004

Reply to Office Action of May 26, 2004

IN THE SPECIFICATION:

Replace the paragraph which begins at line 3 on page 6 and ends at line 22 on page 6 of the application with the following amended paragraph:

The ATCUN motif has been found in other naturally-occurring proteins besides albumins, and non-naturally-occurring peptides and proteins comprising the ATCUN motif have been synthesized. See, e.g., Harford and Sarkar, *Acc. Chem. Res.*, **30**, 123-130 (1997); Bal et al., *Chem. Res. Toxicol.*, **10**, 906-914 (1997); Mlynarz, et al., *Speciation 98: Abstracts*; <http://www.jate.u-szeged.hu/~spec98/abstr/mlynar.html>. Cu(II) and Ni(II) complexes of ATCUN-containing peptides and proteins have been reported to exhibit superoxide dismutase (SOD) activity. See Cotelle et al., *J. Inorg. Biochem.*, **46**, 7-15 (1992); Ueda et al., *J. Inorg. Biochem.*, **55**, 123-130 (1994). Despite their reported SOD activity, these complexes still produce free radicals which damage DNA, proteins and other biomolecules. See Harford and Sarkar, *Acc. Chem. Res.*, **30**, 123-130 (1997); Bal et al., *Chem. Res. Toxicol.*, **10**, 915-21 (1997); Ueda et al., *Free Radical Biol. Med.*, **18**, 929-933 (1995); Ueda et al., *J. Inorg. Biochem.*, **55**, 123-130 (1994); Cotelle et al., *J. Inorg. Biochem.*, **46**, 7-15 (1992). As a consequence, it has been hypothesized that at least some of the adverse effects of copper and nickel *in vivo* are attributable to the binding of Cu(II) and Ni(II) to ATCUN-containing proteins which causes the production of damaging free radicals. See Harford and Sarkar, *Acc. Chem. Res.*, **30**, 123-130 (1997); Bal et al., *Chem. Res. Toxicol.*, **10**, 915-921 (1997); Cotelle et al., *J. Inorg. Biochem.*, **46**, 7-15 (1992). Cf. Koch et al., *Chem. & Biol.*, **4**, 549-60 (1997). The damaging effects produced by a Cu(II) complex of an ATCUN-containing peptide have been exploited to kill cancer cells *in vitro* and to produce anti-tumor effects *in vivo*. See Harford and Sarkar, *Acc. Chem. Res.*, **30**, 123-130 (1997).